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L3: Entry 1 of 3 File: USPT Oct 6, 1998

DOCUMENT-IDENTIFIER: US 5817491 A
TITLE: VSV G pseusdotyped retroviral vectors

DEPR:
The present invention takes advantage of the previously disadvantageous fact that the protein expression level of a gene downstream from the 5' LTR or other promoter, and spaced therefrom by an intervening gene, is substantially less than if the intervening gene were absent. In the present invention, the selectable gene is placed downstream from a gene of the packaging genome or the gene of interest carried by the vector construct, but is still transcribed under the control of the viral 5' LTR or other promoter without any splice donor or splice acceptor sites. This accomplishes two things. First, since the packaging genes or genes of interest are now upstream with no intervening gene between themselves and the promoter, their corresponding proteins (packaging protein or protein of interest) will be expressed at a higher level (five- to twentyfold) than the selectable protein. Second, the selectable protein will be expressed on average at a lower level, with the distribution of level of expression shifting toward lower levels. However, the selection level for resistance to phleomycin remains the same, so that only the top-end expressing cells survive. The levels of the packaging protein or of the protein of interest will still be proportional, only in this case, a higher level of selectable protein corresponds to a much higher level of packaging protein or protein of interest.

DEPR:
In some cases, gene products from other viruses may be used to improve the properties of retroviral packaging systems. For instance, HIV rev protein might be included to prevent splicing of HIV env or HIV gag/pol MLV vectors or HIV sor might increase the infectivity of T cells by free virus as it does with HIV (See Fischer et al., Science 237:868-893, 1987).

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L4: Entry 3 of 6 File: USPT Mar 16, 1999

DOCUMENT-IDENTIFIER: US 5883081 A
TITLE: Isolation of novel HIV-2 proviruses

DEPR:
The gene therapy vectors of this invention typically include at least one "anti-viral agent" or "viral inhibitor" operably linked to an expression control sequence (such as an LTR of the invention). As used herein the terms "anti-viral agent" and "viral inhibitor" refer to any nucleic acid whose product, upon transcription or translation, inhibits the replication of a specified virus. Anti-viral agents are known in the art. The literature describes such genes and their use. See, for example, Yu et al., (1994) Gene Therapy, 1:13; Herskowitz (1987) Nature, 329:212 and Baltimore (1988) Nature, 335:395. Anti-viral agents useful in this invention include, without limitation, anti-sense genes, ribozymes, decoy genes, transdominant genes/proteins and suicide genes.

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L4: Entry 4 of 6 File: USPT Jul 22, 1997

DOCUMENT-IDENTIFIER: US 5650309 A
TITLE: Viral vectors

DEPR:
The vectors of this invention include at least one "anti-viral agent" or "viral inhibitor" operably linked to an expression control sequence. As used herein the terms "anti-viral agent" and "viral inhibitor" refer to any nucleic acid whose product, upon transcription or translation, inhibits the replication of a specified virus. Anti-viral agents are known in the art. The literature describes such genes and their use. See, for example, Yu et al., Gene Therapy, 1:13 (1994); Herskowitz, Nature, 329:212 (1987) and Baltimore, Nature, 335:395 (1988). Anti-viral agents useful in this invention include, without limitation, anti-sense genes, ribozymes, decoy genes, transdominant proteins and suicide genes.

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